THE CARDIFF PENTHRANE INHALER

A Vaporizer for the Administration of Methoxyflurane as an Obstetric Analgesic

BY

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SUMMARY

Twenty Cardiff Penthrane Inhalers tested over a range of ventilation, have delivered concentrations within the limits of 0.35 ± 0.07 per cent methoxyflurane. Five vaporizers submitted to a stringent testing procedure performed within these limits with continuous flows of 5–40 l./min, sine-wave ventilation of 3–20 l./min and a temperature range of 13.5–44°C. The delivered concentration was consistent from the first breath onwards and was substantially unaffected by attitudes of inclination or agitation. The resistance to breathing appeared acceptable to mothers in labour. Sudden changes in ambient temperature may, however, lead to spurious concentrations being delivered, for several minutes. A prototype baffle safely allows oxygen to be added to the inhaled vapour. The vaporizer is considered to be sufficiently robust to be safe for use by unsupervised midwives.

Inhalational drugs have, for many years, played a prominent role in obstetric analgesia. It has long been appreciated that precise control of the inhaled concentration is essential if there is to be satisfactory analgesia without unanticipated oversedation or the risk of unconsciousness. When trichloroethylene was originally introduced for obstetric pain relief, a number of vaporizers proved unsafe. This led the Central Midwives' Board to draw up requirements for the performance of trichloroethylene vaporizers for use by unsupervised midwives.

Methoxyflurane has been shown to have valuable analgesic properties (Boisvert and Hudon, 1962; Romagnoli and Korman, 1962; Johnstone, 1963). It has been demonstrated to have advantages as an obstetric analgesic over both trichloroethylene (Major, Rosen and Mushin, 1966) and nitrous oxide (Jones et al., 1969a, b) under similar conditions. The optimum concentration for intermittent inhalation was found to be 0.35 per cent (Major, Rosen and Mushin, 1967). These authors further demonstrated that 0.45 per cent vapour was too strong and 0.25 per cent was relatively less effective. Rosen and associates (1969), in a field trial comparing the three agents, confirmed the acceptability of methoxyflurane in midwifery practice and found no need for an alternative, lower concentration.

If methoxyflurane is to prove acceptable for use by unsupervised midwives, it must not only be shown to be a safe and effective drug, but, in addition, a reliable vaporizer must be developed for its administration. The requirements of the Central Midwives' Board concerning trichloroethylene vaporizers are explicit (Medical Research Council Report, 1954) and vaporizers embodying the necessary characteristics have proved to be satisfactory in clinical use.

At our request, Messrs Cyprane Ltd have developed a draw-over vaporizer, based on the Tecota Mark 6 which is designed to deliver 0.35 per cent methoxyflurane, but without an alternative, lower concentration. A number of prototypes of this vaporizer, after preliminary tests by us, were used in a field trial (Rosen et al., 1969). The unit, after slight modification, is now commercially available as the Cardiff Penthrane Inhaler.

GENERAL DESCRIPTION OF THE VAPORIZER

The apparatus is a calibrated, temperature-compensated, draw-over vaporizer with a built-in, one-way valve. In outward appearance it is similar to the Tecota Mark 6 inhaler, but it is painted emerald green to match the colour of the methoxy-
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The Cardiff Penthrane inhaler.

1. Air inlet
2. Vaporizer chamber inlet
3. Vaporizer chamber outlet
4. Bimetal strip
5. Felt block
6. Felt wick
7. Reservoir
8. Window
9. Bypass orifice
10. Outlet port

flurane (Penthrane; Abbott Laboratories) bottles. The outer shell is of diecast alloy. The whole of the internal assembly in contact with the saturated vapour is constructed of brass, and not of aluminium as in the Tecota Mark 6 trichloroethylene vaporizer, since methoxyflurane has a corrosive action upon aluminium. The weight of the apparatus is approximately 1.8 kg, which is rather heavier than the Tecota (1.25 kg). The reservoir chamber for liquid methoxyflurane is constructed of copper.

The illustration (fig. 1) shows that the vaporizer is arranged concentrically. Air is drawn in through a number of slots in the edge of the top plate (1), thus discouraging connection to the outflow of any other apparatus. The airstream is then split so that the greater part passes through an orifice (9) set at manufacture, around the inside of the outer casing to the valved outlet port (10). The remainder passes through an orifice (2), down into the vaporizing chamber through the central cavity of a thick, cylindrical, felt block (5). This air then passes through four radial channels in the base of the felt block, rises in the space between the block and the vaporization chamber wall and finally escapes by way of two diametrically opposed identical orifices (3). A flat disc, supported from the vaporizer casting by a bimetal strip (4), overlies each orifice. This assembly constitutes the thermal compensation of the vaporizer. It will be noted that the bimetal strips, being close to the outer casing and in the stream of the mixed air flow, do not necessarily reflect the temperature inside the vaporizing chamber. The felt block, when fully charged, contains 35–40 ml of liquid methoxyflurane. It receives the liquid from the reservoir by capillary attraction up a narrow felt wick (6). The liquid reservoir (7) is so shaped that, even when full, no attitude of the machine will allow flooding of the vaporizing chamber. The level of liquid in the reservoir can be observed through a small glass window (8). It should be noted, however, that because of absorption by the wick, the liquid level may disappear shortly after an initial filling.

The filling device now fitted to the production model (though not to the prototypes) supersedes that on the Tecota Mark 6. This device, the Frazer Sweatman Pin Safety System, makes it impossible to overfill the vaporizer, prevents wastage resulting from spilling the liquid anaesthetic and makes it almost impossible to fill the vaporizer with the wrong liquid. This has been made possible by the standardization of bottle threads and by the development of a keyed bottle adaptor and overfill prevention device. The effectiveness of the device in preventing accidental filling of the vaporizer with the wrong liquid depends on the thread of the Penthrane bottle being incompatible with other bottle threads. The adaptor has been tried on a large number of drug and reagent bottles without a match being found, thus suggesting that the thread has been well chosen.

A one-way valve, consisting of a mica disc and knife-edge seating, is included in the outlet port assembly. When at rest, this valve lies in the partially open position.

The baseplate of the vaporizer is extended beyond the edge of the main casting and suction cups have been provided at each of its corners for greater stability.

The vaporizer is set at 0.35 per cent vapour by the manufacturer and subsequently checked by the British Standards Institute. A dated wax seal is then stamped on the vaporizer. The seal is so
located that it conceals a recessed screw that must be removed if any adjustment is to be made to the settings. Such an adjustment can therefore only be made by destroying the seal.

**ROUTINE TESTING PROCEDURE**

The original body concerned with testing trichloroethylene vaporizers for the Central Midwives' Board was the National Physical Laboratory. Using a standard test procedure, vaporizers were checked before delivery and subsequently annually, in order to ensure consistent performance. The British Standards Institution have now taken over this responsibility.

The production models of the Cardiff Penthrane Inhaler have all been submitted to test by the British Standards Institution. The concentration of each vaporizer is measured at a respiratory rate of 24 per minute, and minute volumes of 7, 10 and 20 l./min. The test sequence is repeated at 20°, 29° and 35°C. If the output is within a range of ±20 per cent of the specified concentration (0.35 per cent) the instrument is then passed for use.

Twenty production models of the vaporizer have been tested by us. Their performance, together with the results of five of them tested in greater detail, is presented below.

**EXPERIMENTAL METHOD**

In these experiments the vaporizers were submitted to a variety of continuous and sine-wave flows. The sine-wave flows were provided by a calibrated piston pump which possessed linkage geometry enabling it to deliver an almost perfect sine-wave flow pattern. It was connected to the vaporizer via an Ambu E non-rebreathing valve. Thus, the vaporizer received no back-pressure, thereby ensuring a unidirectional flow. The frequency of the pump was continuously variable from 7 to 60 cycles per minute and its displacement was adjustable from 250 to 1,000 ml. Continuous flows were provided by a vacuum pump and were monitored with an accurate bobbin flowmeter.

**Sampling technique.**

The vaporizer output was found to exhibit considerable streaming so that the concentration of the anaesthetic vapour was inconsistent across the bore of the outlet orifice. In addition, the concentration was found to vary with instantaneous flow rates, resulting in both axial and diametric non-homogeneity. Moreover, rubber or plastic components in the circuit tend to absorb some of the vapour. In order to overcome these difficulties, a special mixing chamber was evolved, constructed of Quickfit glass components with ground glass taper connections (fig. 2). A spherical flask of nominally 500 ml volume, fitted with an internal fan which was driven by a flexible drive, was found necessary to ensure homogeneity of the vapour.

**Fig. 2**

Sampling system.

1. Vaporizer 4. All-glass syringe
2. Glass mixing chamber 5. Inflating valve
3. Seal 6. Piston pump

**Analysis of samples.**

Samples of 5 ml of the vapour were drawn into all-glass syringes coincident with inspiration (though this precaution was found later not to be necessary). The samples were analyzed using a Pye Series 104, Model 4 gas chromatograph. Each sample was immediately transferred to a gas sampling valve fitted with a 0.5-ml sampling loop which ensured reproducibility of sample size. The output of the chromatograph was recorded on a Vitatron Model UR 400/2M integrating recorder.

**Preparation of standards.**

Gas standards were prepared by vaporizing an accurately weighed quantity of methoxyflurane in an 11-litre sealed, glass aspirator bottle equipped with nylon taps. After shaking the container for approximately 10 minutes, three 5-ml samples
were withdrawn and analyzed. The peak area was recorded. Usually, the three samples gave identical peaks. When this was not so, the standard container was further agitated until successive peaks were identical. The coefficient of variation for successive samples of the same standard was \( \pm 0.92 \) per cent and the coefficient of variation of five separate standards was \( \pm 0.82 \) per cent.

**RESULTS**

*Continuous flow characteristics.*

The vaporizer is designed for use only as a draw-over machine for connection directly to the patient and not for continuous flow. However, it was felt that knowledge of its performance under continuous flow conditions might help to explain its performance with sine-wave flows.

Five vaporizers were selected at random from the twenty available. For any given flow, the run was continued only long enough to ensure that the mixing chamber was flushed before sampling. Vaporizers were allowed to stand for 20-30 minutes between each run in order to avoid effects due to cooling.

The concentration delivered varies considerably over the range tested thus underlining the unsuitability of the vaporizer for use with continuous flows (fig. 3). The maximum concentration is 0.44 per cent vapour at a flow of 15.1 l./min from which there is a precipitous decline with decreasing flow rates, and a gradual fall with increasing flows. The significance of this is apparent when the response of the vaporizers to sine-wave flows is considered.

*Sine-wave flow characteristics.*

The regulations governing the performance of trichloroethylene vaporizers specify a range of ventilation within which the instrument should continue to deliver vapour inside the specified range of concentrations. The five Cardiff vaporizers were tested with sine-wave flows at frequencies of 7, 20, 40 and 60 breaths/min, tidal volumes of 250, 500, 750 and 1,000 ml, and all combinations of these values. The total ventilation varied, therefore, from 1.75 to 60 l./min and therefore peak flows of 5.5-188 l./min \((\pi \times \psi)\).

The results are shown in figures 4 and 5. Alteration of either tidal volume or frequency while keeping the other factors constant reveals no consistent effect by either parameter upon the concentration delivered (fig. 4). However, when the total ventilation in each case is calculated and plotted against delivered concentration, the pattern of distribution is similar to that of the continuous flows (fig. 5). In this instance, the maximum concentration occurs at a minute volume of 6 l./min compared with a continuous flow of 15 l./min. If one calculates the mean unidirectional flow \((i.e. 2 \times \text{minute ventilation})\) for each of the sine-wave ventilation rates, the two responses correspond so closely (fig. 6) that it would be feasible to use continuous flows for checking this vaporizer.

**Temperature compensation.**

(1) *The effect of time.* Five vaporizers were each submitted to a continuous run of 30 minutes with a frequency of 20 b.p.m. and a 500-ml tidal volume. In addition, on one vaporizer, the test was repeated using tidal volumes of 250 and 1,000 ml while the frequency was maintained at 20 b.p.m. (fig. 7).

It can be seen that the temperature compensation provided does not entirely overcome the progressive cooling of the vaporization chamber due to the latent heat of vaporization of methoxyflurane. This may be attributed, possibly, to the poor thermal conductivity of the felt block and to the location of the thermostats in the bypass stream, causing them to respond more to ambient temperature than to the temperature within the vaporization chamber.

It must be remembered, however, that the vaporizer is not intended for this duration of uninterrupted use but, rather, for intermittent administration. There would normally be a pause between successive episodes of inhalation that might be expected partially to restore the delivered concentration to its original level. To test this, one vaporizer was submitted to intermittent ventilation in a variety of patterns chosen to approximately simulate normal clinical usage such as we have observed to be common during the later stages of labour. The response of the vaporizer to inhalation periods of 1 minute separated by rest periods of 3 minutes is presented in figure 8. The vaporizer can be seen to have performed more consistently under these circumstances.

(2) *The effect of changes in ambient temperature.* Two vaporizers were placed in thin poly-
FIG. 3
Relationship between vapour concentration and continuous flow.

FIG. 4
Relationship between vapour concentration and sine-wave flow (simulated breathing with various tidal volumes and frequencies).

FIG. 5
Relationship between vapour concentration and sine-wave flow (simulated breathing with various minute volumes).

FIG. 6
Relationship between vapour concentration and ventilation.

FIG. 7
Relationship between vapour concentration and time.

FIG. 8
Relationship between vapour concentration and patterns of ventilation.
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Theene bags and immersed in a water bath. Arrangements were made to ensure that the air entering the vaporizers was at bath temperature. Water bath, inflow and outflow air temperatures were monitored using the needle probes of a thermistor electrical thermometer. After cooling to 10°C, the bath temperature was elevated in steps of 10°C, and sufficient time was allowed to elapse at each step to ensure that the vaporizer was at an even temperature throughout. The adequacy of this 45-minute time lapse was checked by demonstrating absence of hysteresis of response when the temperature programme was reversed. The maximum temperature reached was about 50°C. At the end of the equilibration time at each step, each vaporizer was run at 20 b.p.m. and a tidal volume of 500 ml for sufficient time to allow for duplicate samples.

The responses of the two vaporizers are shown in figure 9. The thermostat mechanism maintained the concentration within the limits of 0.35 ± 0.07 per cent (i.e. a ±20 per cent variation) for a temperature range of 13.5–44.0°C, and achieved a maximum concentration of 0.4 per cent at 30°C. Beyond this range, in either direction, the concentration delivered became weaker.

Because of the construction of the vaporizer, there might be delays in equilibration of the central core temperature resulting from acute changes in ambient temperature. The hysteresis noted during the preliminary runs of the above experiment suggest that spurious concentrations might be delivered during the period immediately following a sudden change in ambient temperature. Such changes might easily be envisaged in practice, if the vaporizer were kept in a cupboard that includes heating pipes, or on a sunny windowsill. Alternatively, storage in a car during cold weather would result in the opposite extreme being encountered. Subsequent immediate use might result in temperature gradients that would interfere with the proper functioning of the compensating mechanism.

In order to test this, one vaporizer was placed in a refrigerator at 4°C overnight, and two others were left in a water bath at 50°C, for sufficient time to allow thermal equilibrium to be established. The three vaporizers were then transferred simultaneously to ambient temperature (21.5°C) in air. The cooled vaporizer and one of the warmed ones were then subjected to runs of 30 seconds every 5 minutes with a tidal ventilation of 500 ml and a frequency of 20 b.p.m. The third (warmed) vaporizer was sampled similarly but at 20-minute intervals in order to see if there was any significant cooling effect due to the ventilation that the other two were receiving. There was no difference between this and the other warmed vaporizer; its performance has therefore not been included in the results.

The responses of the vaporizers are shown in figure 10. The concentration of vapour delivered by the vaporizer that started at 4°C has gradually increased to enter the accepted range after 35 minutes and has achieved its final concentration after 85 minutes. The vaporizer that was cooling from 50°C, however, responded to being presented with a 28.5°C temperature difference by an initial rapid increase in concentration to pass directly through the tolerated range and exceed the 0.42 per cent limit for a period that extended
between 10 and 90 minutes after removal from the water bath. It finally reached equilibrium after 105 minutes.

This response can be explained by a gross discrepancy between the thermal time-constants of the outer bypass chamber (containing the thermostats) and the felt block in the brass vaporization chamber. Thus, the inner vaporization chamber cools more slowly, maintaining a high vapour pressure for methoxyflurane while the thermostats cool more rapidly, thereby opening and allowing a high concentration to be delivered.

The effect of different attitudes of inclination.

The five vaporizers were run for 30 seconds with sine-wave ventilation of 500 ml tidal volume and a frequency of 20 b.p.m. After a rest period, each was run at 45° from the vertical attitude and then at 90°. This produced no consistent change in the delivered concentrations of the vaporizers, and the standard deviations were no greater than when the vaporizers were vertical. Even when inverted, no liquid anaesthetic was seen to leak out from any of the vaporizers.

The effect of shaking.

After having been run for 30 seconds and sampled with the ventilation as indicated above, each of the five vaporizers was shaken vigorously for a further 30 seconds. A repeat run performed immediately after this manoeuvre revealed no consistent change in concentration though the standard deviation was slightly larger after shaking than before (± 0.036 per cent compared with ± 0.013 per cent respectively).

The first breath.

The vaporizers are intended for intermittent use. It is possible that the first breath delivered from a vaporizer that has been left at rest for some time might differ significantly from the mean concentration delivered. This might come about if saturated vapour from the vaporization chamber were to diffuse out into the bypass section while at rest.

By removing one of the retaining screws of the outlet port, a fine nylon catheter was passed into the bypass section of three vaporizers that had been allowed to stand for various periods of time. Concentrations up to but not exceeding 0.35 per cent were found.

The mean concentration delivered during the first breath was tested by applying a Wright meter to the outlet of each vaporizer, using its turbine as a means of mixing the stream, and then sampling distal to this throughout the inspiratory phase of the sine-wave pump. There was some variation in the output, but no consistent differences were noted between the concentration of the first breath and the mean running concentrations.

Resistance to breathing.

Mothers in labour tend to hyperventilate. Whatever the reasons, the degree of hyperventilation is frequently considerable. Major, Rosen and Mushin (1967) measured the ventilation during the last half-hour of labour using a Wright meter. They found that, during contractions, total ventilation was of the order of 15-20 l./min, with a maximum sustained level in one patient of nearly 30 l./min.

Using a Greer ventilation computer with a Lilly type pneumotachograph head calibrated to continuous flows of 300 l./min, we have measured peak inspiratory flows as high as 300 l./min when the patient breathed only through a mask and pneumotachograph screen.

Figure 11 shows the inspiratory and expiratory flow-pressure curves for five inhalers complete with hand-set expiratory valves. For a mother to produce peak flows of 200-300 l./min she would have to generate pressures in excess of 40 cm H₂O.
when using this vaporizer. We have found that when patients were breathing with peak flows of about 250–300 l./min, connection to the vaporizer caused an immediate fall in peak flow to approximately 100 l./min; the mother thus generated a pressure of 8 cm H₂O. However, mothers did not object to this degree of restriction; indeed, tidal ventilation was generally unaffected by the introduction of the vaporizer resistance.

One-way valve characteristics.

The complete inhaler consists of the vaporizer, a length of corrugated rubber hose, a valved hand-set and a mask. Unidirectional flow through the vaporizer is achieved by the provision of two unidirectional valves. Both valves are constructionally and dimensionally similar. Each consists of a light plastic disc trapped in a metal cage which overlies a circular knife-edge seating. The disc in each case is free and not acted upon by a spring. One valve, situated in the outlet port assembly, acts as a one-way valve preventing the passage of air into the vaporizer through the expiratory port. The second valve is fitted into the hand-set and acts as an expiratory valve. With the mother lying supine, the hand-set is held horizontally with the result that the expiratory valve lies so that, when there is no flow, it is partially open. The same applies to the other valve when the vaporizer is vertical. Therefore, if flows insufficiently large to operate the valves were to be generated, a multidirectional system might be produced. This would have a number of consequences. Failure of the expiratory valve would cause air to be drawn in through it during inspiration, bypassing the vaporizer, resulting in a low inspired concentration. Failure of the other valve would cause rebreathing and the reverse flow through the vaporizer would cause two further effects. Increased heat loss due to latent heat of vaporization might overcome the capacity of the temperature-compensating mechanism. Further, at the end of expiration, some air which already contained the appropriate amount of vapour, passing back into the vaporizer would pick up further vapour so that the next inspiration would consist, initially, of excessively strong vapour. Clearly the performance of the complete inhaler depends heavily on the proper functioning of the valves.

A number of vaporizers were tested by applying a slowly increasing reverse flow to each outlet port until the partially open valve suddenly closed. The flows necessary to achieve this varied considerably with each valve, depending, presumably, upon the starting position of its disc. Reverse flows as high as 14 l./min were encountered when the vaporizer was standing on a flat surface. Similar reverse flows were found with the expiratory valves when the hand-set was in the horizontal position.

When complete inhalers were tested with sine-wave flows, however, the performance was unaffected by the valve characteristics except at very low flows when lower concentrations were produced than when the vaporizers were tested alone with an Ambu E unidirectional valve. It would appear, therefore, that except in extreme circumstances, the unidirectional flow characteristics are adequate.

Loss of methoxyflurane by evaporation.

Six vaporizers were filled. Two were sealed with aluminium foil caps which covered both inlet and outlet orifices, a further pair were sealed similarly but only at the outlet port and the final pair, which acted as controls, were unsealed. All six were placed on a shelf in a moderately ventilated, large room with an average ambient temperature of approximately 21°C. Each vaporizer was weighed daily. The average loss by evaporation per week amounted to 12.2 ml of liquid methoxyflurane when both orifices were left open, 6.1 ml when the exit port was sealed, and 4.8 ml with both ports sealed. In contrast, a mother inhaling 0.35 per cent methoxyflurane at a minute volume of 15 l./min for 1 minute in 3 over a period of 1 hour would use something like 5–6 ml of liquid methoxyflurane. Thus the loss by evaporation is economically significant; it could be halved by the provision of a removable plug on the outlet port.

Production spread.

As an indication of the production spread of the calibrated vaporizer, twenty consecutive production models were submitted to a 6-minute sequence of sine-wave ventilation. At the end of each minute, the output of the vaporizer under test was checked and the tidal volume was then
immediately adjusted in the sequence shown in table I. Thus, each vaporizer was tested for a range of sine-wave ventilation of 4–12 l./min and, by comparing the first and last readings, the stability of the compensating mechanism with respect to time could be assessed. The mean concentration delivered by the twenty vaporizers at the end of each minute together with the standard deviations is shown in table I. The observed variation of the twenty vaporizers was 0.399–0.281 per cent. This range is within the permitted ±20 per cent variation.

**TABLE I**

<table>
<thead>
<tr>
<th>Minutes elapsed</th>
<th>Tidal volume (ml)</th>
<th>Mean concentration (% v/v)</th>
<th>Standard deviation (%)</th>
<th>Coefficient of variation (%)</th>
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<tr>
<td>1</td>
<td>400</td>
<td>0.371</td>
<td>0.018</td>
<td>5.1</td>
</tr>
<tr>
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<td>0.016</td>
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<tr>
<td>6</td>
<td>400</td>
<td>0.356</td>
<td>0.018</td>
<td>5.2</td>
</tr>
</tbody>
</table>

Frequency 16 cycles per minute.

**Robustness.**

Prototype vaporizers used during the field trial were tested at intervals throughout the trial with the above procedure and were found to retain their calibration over a period of constant use lasting approximately six months. Several of the prototypes showed signs of having been dropped on to hard floors and bore other evidence of enthusiastic usage. One vaporizer which had inadvertently been immersed in near-boiling water, also retained its calibration, after a period of drying out. In general, it would appear that the instrument is sufficiently robust to tolerate most physical insults that might be encountered under normal conditions of operation without a significant change in delivered concentration.

**Device for augmenting the inhaled oxygen concentration.**

At our suggestion a device for adding oxygen to the inhaled mixture has been designed by Messrs Cyprane Ltd. A prototype which has been tested consists of a head fitting over the vaporizer inlet into which oxygen flows through a nozzle (fig. 12). The oxygen concentrations delivered by the device were measured with a Servomex oxygen analyzer (OA150) while ventilating the vaporizer with a sine-wave pump.

The back-pressure developed by the nozzle reached 15 Lb./sq. in. at 5 l./min and at higher flows the tubing blew off the connector, thus limiting the maximum flow to 5 l./min. Flows of oxygen between 1 and 5 l./min were tested. The performance of the device with sine-wave ventilation is shown in figure 13. Varying the frequency independently of the total ventilation had very little effect upon the oxygen concen-
trations achieved. The device was designed to give a maximum output of about 50 per cent oxygen—which is the level available with other accepted methods. Since there is no rebreathing through the vaporizer, the presence of the device can have no deleterious effect if the oxygen runs out. Any increase in resistance to respiration that it caused was negligible.

CONCLUSIONS
The five Cardiff Penthrane Inhalers that have been tested delivered the specified concentration of 0.35 per cent with a range of ±20 per cent under a wide variety of environmental conditions. However, additional studies show that, in certain extreme circumstances, a spuriously high concentration can be delivered after the vaporizer has been removed from a hot environment into a cool one and that this persists sufficiently long for it to be of possible clinical significance. This risk, if unavoidable, should be brought to the attention of its users in order that they may take the necessary precautions. By covering the outlet port when the vaporizer is not in use the daily loss of methoxyflurane by evaporation may be halved.

REFERENCES
Medical Research Council (1954). Memorandum No. 30. The use of Trilene by midwives by the Committee on Analgesia in Midwifery. H.M.S.O.